Book Reviews

The Trouble with Medical Journals, by Richard Smith, M.D., 292 pp, softcover, $39.95, ISBN 1-85315-673-6, London, UK, Royal Society of Medicine Press, 2006.

Richard Smith practiced medicine for several years, then worked for the *British Medical Journal* for 25 years, 13 of them as editor-in-chief and chief executive of the *BMJ* Publishing Group—a superlative background.

Unlike Marcia Angell, M.D., and Jerome Kassirer, M.D., former editors of the *New England Journal of Medicine (NEJM),* who were concerned with medical misinformation in general,[1,2] Smith addresses the many unavoidable conflicts in medical journals: flaws in "Big Pharma"-sponsored studies, as well as author bias and fraud as separate issues, the business aspects of journal publishing, and a possible future with Web-based reports and no print journals as we know them now.

Serious as it is, with academic referencing and a proper index, *TMJ* is as humorous as it is informative. For an example of both seriousness and humor in the same paragraph (p 239): "But generally complaints are more useful [than compliments]—because they provide a direct route to action. We usually [at the *BMJ*] had around 30 or 40 a quarter to analyse, but every so often we hit the jackpot. We had over one hundred when we got Mozart's birthday wrong, around 150 when our imaginative Irish columnist seemed to advocate running over cats, and almost 200 when we produced an issue of the *BMJ* as it might look in 20 years' time. 'It was like a favourite aunt turning up drunk and in drag,' wrote one correspondent." Cambridge University Press wanted the humor removed, hence Smith moved to the RSM Press.

Some history of scientific journals is given, with emphasis on medical journals, and the *BMJ* got special attention, of course. *BMJ's* studies on peer review "... [have] shown that it is slow, expensive, ineffective, something of a lottery, prone to bias and abuse, and hopeless at spotting errors and fraud." "If it were a drug it would never get onto the market (p 8)."

Later tests at the *BMJ* showed that peer review gave almost the same result as editor review. A case was also made for paid professional peers for review, and the *BMJ,* unusually, does pay £50 for a review that takes two hours on average (p 86). Smith admitted that the cachet of peer review was too strong to expect any significant change. On the positive side, he wrote that it does lead to improvement in papers, both in more complete acknowledgement of earlier work and in clarity. "It wasn't long ago that many journals and grant-giving bodies did not send back reviewers' comments. They would simply reject without explaining why, fearing that sending reasons would only encourage authors to disagree and appeal—so creating more work" (p 87). But there are now journal ombudsmen and appeal committees, and there is a pecking order of journals, so any reasonable-looking work will be published somewhere, according to Smith.

The importance of medical journals is confirmed. Few people read whole papers, but the prestige of the journal leads to quotations from abstracts in press releases and advertisements that the public sees. The Big Five *(Ann Intern Med, BMJ, JAMA, Lancet, NEJM)* are highly profitable. Multiple reprints of single papers to be handed out as advertising, usually for new drugs, may bring in $1 million each, and constitute a major fraction of journal income. It's no surprise that reprints of the VIGOR trial of rofecoxib were the key example. Smith wrote that the *NEJM* may have been partially guilty for not questioning the interpretation of the fourfold increase in myocardial infarction with rofecoxib compared with naproxen (p 28). Other examples were given. A survey of UK doctors showed that they trusted journals more than "the government" or the National Health Service (p 50).

A chapter said to be hardest to read, although I did not find it so, pointed out that the flaws in clinical and observational trials are the basis for most of the flaws in medical papers. A discussion of these flaws goes far beyond mine.[3] Regression to the mean in measurements such as blood pressure, flaws in risk adjustment, failure to compare new treatments with something besides placebo, and other factors are all presented. "This pattern of studies of a series of patients suggesting benefits from a treatment and randomized trials, showing no benefit or even harm, is repeated time and time again" (p 73).

Research misconduct gets a thorough airing. The *BMJ* has been known to alert a would-be author's institution to the possibility of fraud, and has been the target of some lawsuits itself. The existence of the Committee on Publication Ethics (COPE) is a self-help group for editors (p 105). Ghost writing and figurehead authorship is discussed (p 120), as are multiple publications of similar papers, a clear waste of resources and time, and its corollary, non-publication of negative findings. Redundant publication is potentially dangerous when meta-analyses combine many versions of what is actually the same study (p 121).

As Smith wryly notes, editors have been less likely to police themselves than others, but there is now the World Association of Medical Editors (WAME) (p 145) that can do just this. "Grandiosity and self-importance are ... occupational hazards of editors. Many associations go on with poorly performing editors for fear of the fuss that might result from firing him or her. One way to avoid this predicament is to give the editor a fixed-term contract, usually for 5 years, and that is what we did with the editors of the *BMJ* journals" (p 146-154). Smith notes that some journals, notably *JAMA,* have a "firing culture," and that *NEJM* and *CMAJ* are not immune.

The reasons for firings are usually not technical incompetence, but failure to kowtow to commercial interests. "Most editors of the world's 10,000 or so biomedical journals have received no training. One day you're a professor of cardiology; the next you're editing a journal…. For an editor with no training in cardiology to become a cardiologist overnight would be unthinkable, but it's routine the other way round" (p 151). There is no college of editors, but such would clearly be desirable. British journals appoint professional editors who have come up through the ranks, and Smith thinks American journals would do well to imitate them.

Much of the editor's worry is about publishing articles on studies that lacked informed consent or ethics committee examination (p 163). This includes quotations of papers in the mass media of negative studies (p 178) as being abusive to participants' psyches. Future worries may be accommodating to online publication only for a stiff author fee (p 220). This might eliminate fine work by individual practitioners and astute reviews by retirees.

Among the few disappointing features is the book's unqualified praise for PubMed, without a comment that while a number of popular but mostly nonmedical

magazines are abstracted, only 10 percent of medical journals are. The omissions include this journal, *Fluoride*, the *Journal of Orthomolecular Medicine*, and the *Journal of Nutritional and Environmental Medicine.* Also the book seems not to recognize radiation hormesis (p 18);[4] dismisses the link between MMR vaccine and autism (pp 18-23);[5] strongly supports the idea that HIV causes AIDS (p 60), a mistake, in my opinion;[6] and accepts without skepticism the conventional view of the hazards of moderately elevated blood pressure, which has been debunked.[7]

Aside from these subjects it would be hard to imagine a more subtle, sagacious, even-handed concatenation of the multifaceted problems of medical journals and their editors. It is most highly recommended! Especially for reporters.

1. Kauffman JM. Book Review: *On the Take: How America's Complicity with Big Business Can Endanger Your Health*, by Jerome Kassirer. *J Am Phys Surg* 2005;10:25-26.
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4. Orient JM. Book Review: *Under-Exposed: What if Radiation is Actually GOOD for You?*, by Ed Hiserodt. *J Am Phys Surg* 2006;11:32.
5. Goldman GS, Yazbak FE. An investigation of the association between MMR vaccination and autism in Denmark. *J Am Phys Surg* 2004;9:70-75.
6. Bauer HH. Demographic characteristics of HIV: III. Why does HIV discriminate by race? *J Sci Exploration* 2006;20:255-288.
7. Kauffman JM. *Malignant Medical Myths*. West Conshohocken, Pa.: Infinity Publishing; 2006:109-123.

Joel M. Kauffman, Ph.D.
Berwyn, Pa.

Minutemen—The Battle to Secure America's Borders, by Jim Gilchrist and Jerome R. Corsi, Ph.D., 375 pp, hardback, $25.95, ISBN-13: 978-0977898411, Torrance, Calif., World Ahead Publishing, 2006.

This book by Jim Gilchrist, founder of the Minuteman Project, and Jerome Corsi, coauthor of *Unfit for Command,* documents the significant harm to our country from the illegal alien invasion, and reasons why our government doesn't want to stop it.

The Minutemen are a group of citizen volunteers who do not engage in confrontations, apprehension, or detainment of illegal aliens, but position themselves along U.S. borders to observe and report unlawful activity to the understaffed U.S. Border Patrol. The Minutemen have been maligned, even by President Bush, who referred to them as "vigilantes."

They estimate that there are up to 30 million illegal aliens in this country. By 2025 there could be 100 million. The authors ask how our country of 300 million can assimilate such an enormous number of poor, uneducated, and predominantly Spanish-speaking people who have broken our laws and remain loyal to their nations of origin.

Just as American colonial essayist Thomas Paine, in his essay *Common Sense*, made the case for our nation's birth, I think this book makes the case on how to prevent its death. The authors believe that our country is slated for demolition. The radical Left, economic globalists including President George W. Bush, and some prominent members of the Roman Catholic Church have the common agenda of eliminating our national borders. This would transform our nation into a Third World country or the "North American Union," an amalgamation of Mexico, the United States, and Canada.

The authors say the liberal media and politicians pander to Hispanics because they're the largest activist minority group in this country. The authors attack the propaganda that Americans should accept these illegals as benign, hard-working people who "do the jobs that Americans won't do." Using a "Trojan Horse" analogy, they state that we are also allowing entrance to terrorists, murderers, rapists, international gang members, and drug traffickers, who sneak in with those hard workers.

We also are exposed to infectious diseases that had been rare or eradicated in this country, such as multi-drug resistant tuberculosis, Hansen's disease, polio, dengue fever, and Chagas disease.

Illegal workers accept slave wages—still more than they would earn at home—creating a "21st-century slave trade" that undermines wages of our own working poor. Uneducated, impoverished, and unassimilated, they become an enormous burden on our social services, hospitals, schools, and prisons.

Without addressing this impact of illegal immigration, it appears to be futile to try to solve any major U.S. domestic problem, such as homeland security, poverty, rising costs of medical services, the "uninsured," illegal drugs, increasing taxes, the national debt, violent crime, expanding prison populations, and crowded, failing public schools. No politician should be allowed to pretend to have solutions for these domestic problems without addressing the real crisis: our open borders and lack of immigration law enforcement. No employer can justify hiring illegal aliens as cheap labor for selfish economic gain, the authors maintain, when the taxpayers have to subsidize an unlimited influx of poor illegal aliens.

The book discusses many facets of the illegal alien issue that are rarely, if ever, addressed by the national media. These include: the concept of Aztlan, the mythical homeland of the Aztec people, which includes a large chunk of the U.S.; Reconquista, the movement to reclaim part of the U.S. for Mexico; matricular consular cards, Mexican identification cards for illegal aliens in the U.S.; and dual citizenship, whereby Mexicans who become U.S. citizens retain their Mexican citizenship and can vote in Mexican elections.

Other topics include chain migration; Social Security "no match" letters, which inform employers about fraudulent Social Security numbers used by employees; and the misinterpretation of the Fourteenth Amendment that results in "anchor babies." Impediments to law enforcement include sanctuary cities and sanctuary laws that prohibit police from determining someone's immigration status. The U.S. crime problem is exacerbated by the MS-13 gang, a violent international Hispanic gang that has infiltrated 34 states. The economic impact of illegals is magnified by EMTALA (the Emergency Medical Treatment and Active Labor Act), which bankrupts hospitals by requiring them to provide free medical care.

Mexico has great economic resources. For example, the Cantrell oil field, the second-largest oil-producing field in the world, belongs to Mexico.

According to the authors, some of the organizations that facilitate illegal aliens in the U.S. are La Raza ("The Race"), Movimiento Estudiantil Chicano de Aztlan (MEChA, a group of Chicano Nationalists), the Ford Foundation, the Mexican American Legal Foundation (MALDEF), the National Immigration Law Center, the American Civil Liberties Union (ACLU), George Soros's Open Society Institute, and the Southern Poverty Law Center, along with other left-wing, anti-American organizations. According to a chapter about Cardinal Roger Mahony of Los Angeles, the cardinal reportedly thinks charity for Mexico's poor should begin with their illegal immigration to the U.S., since apparently they are not the responsibility of the Mexican government.

The authors make it clear that any new laws or regulations concerning "amnesty," a "pathway to citizenship," or "guest worker" programs put forth in a "comprehensive immigration bill," would only stimulate production of more fake documents and identity theft. They believe such proposals will further increase the flow of illegal aliens who will stay and never go back, since nothing, as usual, will be done to secure the borders or enforce new or old immigration laws.

To borrow from Thomas Pain's *Common Sense*—in which he said, "A government which cannot preserve the peace, is no government at all"—I would sum up the message of the book in this way: a government that cannot secure our borders and enforce our laws is no government at all. Or, to quote President Reagan, "A nation without borders is not a nation."

Elizabeth Kamenar, M.D.
Mountaintop, Pa.

Overdose: How Excessive Government Regulation Stifles Pharmaceutical Innovation, by Richard A. Epstein, 296 pp, hardcover, $30, ISBN 978-0300116649, New Haven, Conn., Yale University Press, 2006.

Dr. Richard Epstein has written what is probably the most comprehensive summary of government's disincentives to pharmaceutical innovation. His book deals with both present day concerns and the reforms proposed to alleviate them.

Dr. Epstein examines conflicts of interest between private, public, and bureaucratic parties in research, research funding, patents and intellectual property, FDA regulations, and product liability. Because of the disincentives that face system administrators, Dr. Epstein finds that most current and proposed government interventions harm the very people they were intended to help—the desperately ill.

For example, FDA examiners are called before Congress if a drug they approve has significant side effects. Since every drug has some side effects, each approval carries the risk of censure.

On the other hand, the FDA is rarely, if ever, praised for fast-tracking life-saving drugs. Consequently, in the interests of self-preservation, FDA reviewers tend to withhold or delay approvals, even of breakthrough drugs. Meanwhile, people who would have benefited from the new drugs die prematurely.

Dr. Epstein also effectively dispels common misperceptions about drug companies, especially those concerning pharmaceutical marketing. Many people erroneously believe that the high cost of pharmaceuticals is the result of advertising, because budgets for marketing often exceed research costs. Dr. Epstein, however, walks the reader through what economists call the "Wal-Mart effect." If companies do not advertise, their innovative products will be sold to fewer people. The product must then be priced high in order to recover costs. However, if advertising is allowed to expand the market, the number of buyers increases, and the price needed to recover costs, including marketing costs, decreases. High-volume sales mean that prices go down, not up. From the consumer's standpoint, advertising not only pays for itself, but makes life-saving and life-enhancing drugs more affordable.

Indeed, as a former pharmaceutical research scientist, I witnessed the heartbreak of seeing breakthrough drugs abandoned because the market for them was too small to recover costs. Curtailing advertising, thereby shrinking market size, would mean that even fewer treatments become available to consumers. Most people never anticipate this outcome; that is why Dr. Epstein's thorough treatment of both ethical and unethical marketing practices, including over-promotion and deceptive advertising, is so valuable.

The final chapters describing the legal liabilities imposed upon drug manufacturers made me wonder why any firm is still introducing new drugs. Every drug has some side effects, and courts are making it easier for plaintiffs to prevail, even with all of the warnings that manufacturers are required to provide. Dr. Epstein's review of some landmark cases, such as the Vioxx proceedings, made me realize how poorly the news media has informed readers of many pertinent issues in these trials.

Dr. Epstein usually concludes that those who need pharmaceutical intervention benefit most from market-based solutions, such as property rights and enforceable contracts. Although he relies primarily on economic principles rather than empirical data, Dr. Epstein walks the reader through them, so that the eventual outcome of each current and proposed practice becomes obvious even to the neophyte. However, the academic tone of the writing requires a bit more focus than the casual reader may want to invest.

Those who prefer their economic theory coupled with empirical data may be disappointed in *Overdose*. A wealth of studies confirms Dr. Epstein's well-reasoned conclusion that the marketplace generally outperforms regulation in optimizing not only pharmaceutical innovation, but consumer well-being. Unfortunately, he rarely cites these confirming studies.

Had he reviewed the empirical data supporting his thesis, Dr. Epstein might have started his book with a somewhat different formulation. In Chapter 1, he reminds the reader that the first half of the 20th century saw an increase in life expectancy from 47 to 68 years, a gain of 21 years. In the second half of the 20th century, life expectancy increased to 77, a gain of only 9 years. He concludes that science has already harvested the "low-hanging fruit." Consequently, he believes that future research "will never be able in human terms to duplicate the heroic advances that started 100 years ago."

Given the title of Dr. Epstein's book, it is curious that he did not at least consider the possibility that excess regulation might have already strangled innovation enough to account for at least part of this slowdown in our ability to extend life. After the passage of the 1962 Kefauver-Harris Amendments to the Food and Drug Act, several researchers reported that the introduction of new drugs, especially life-saving innovations, plummeted 50–70 percent.[1-4] Pharmaceutical innovations that did make it to the marketplace were delayed an additional decade in order to meet new FDA requirements.[5] Regulatory rulings stemming from the 1962 Amendments delayed the public's access to life-saving information about significant new uses for nutrients and over-the-counter drugs, sometimes for several decades. Vitamin companies, for example, were forbidden to advertise the ability of folic acid to prevent birth defects.[6] The beneficial effects of aspirin in cardiovascular diseases could not be mentioned.[7]

Had Dr. Epstein considered the literature on pharmaceutical regulation and its impact on innovation in the second half of the 20th century, he might have considered the possibility that low-hanging fruit, especially new uses for products already on the market, may still be within our reach. He might have concluded that excess regulation has already shortened our lives by making this fruit difficult, if not impossible, to pick. This conclusion is more consistent with Dr. Epstein's primary thesis, and gives readers added incentive to take the book's recommendations to heart.

The paucity of empirical data and the academic tone of the presentation are minor defects compared to the book's comprehensive portrayal of the regulatory, bureaucratic, and misinformation hurdles that discourage pharmaceutical innovation. *Overdose* is a "must read" for anyone contemplating reform of pharmaceutical policy. Without this crucial information, many proposed reforms will become a toxic overdose to the industry whose mission is to extend the length and quality of our lives.

Mary J. Ruwart, Ph.D.
Sci-Scource, Burnet, Tex.

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